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CLAIMS

1. A compound of Formula I

wherein R¹ is

$$R^3$$
 $(A)_m$
, R^4
 $(A)_m$
, R^4
 $(A)_m$
, R^7
 $(A)_m$
, R^7
 $(A)_m$
, R^7
 $(A)_m$
, or $(A)_m$
, or $(A)_m$

R³ is hydrogen,

C₁-C₆ alkyl,

- $(CH_2)_n$ aryl, or

-(CH₂)_n heteroaryl;

10 R^4 is C_1 - C_6 alkyl,

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- $(CH_2)_n$ aryl, or

-(CH₂)_n heteroaryl;

R⁵ and R⁶ are each independently hydrogen,

C₁-C₆ alkyl,

15 $-(CH_2)_n$ aryl, or

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-(CH₂)_n heteroaryl;

R⁷ is C₁-C₆ alkyl,

-(CH₂)_n aryl, or

- $(CH_2)_n$ heteroaryl;

each n is independently 0 to 6;

each m is independently 0, 1, 2, or 3;

A is alanine, leucine, isoleucine, proline, phenylalanine, glycine, tyrosine, serine, threonine, tryptophan, cysteine, methionine, valine, asparagine, glutamine, aspartic acid, lysine, glutamic acid, arginine, or histidine;

each RQ is independently hydrogen or C1-C6 alkyl;

 R^2 is -(CH₂)_n-Z; and

Z is aryl, heteroaryl, cycloalkyl, C_1 - C_6 alkyl, O

$$\begin{array}{c} & & \\ & \\ \end{array} , \begin{array}{c} & \\ & \\ \end{array} , \begin{array}{c} & \\ & \\ \end{array} (CH_2)_n \\ & \\ & \\ (CH_2)_n \end{array})_{R^Q)_n} \\ \end{array}$$

 $(CH_2)_n$ $(CH_2)_n$ $(RQ)_n$ $(RQ)_n$ $(RQ)_n$

aryl, substituted heteroaryl, or substituted cycloalkyl, and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

2. A compound according to Claim 1 wherein R¹ is

3. A compound according to Claim 1 wherein R¹ is

$$R^{7}O$$
 $(A)_{m}$,

m is 0, and R^7 is $-(CH_2)_n$ aryl.

5 4. A compound according to Claim 1 wherein R¹ is

m is 0, and R⁷ is -CH₂ aryl.

- 5. A compound according to Claim 1 wherein R^2 is -(CH₂)_n aryl.
- 6. A compound according to Claim 5 wherein aryl is phenyl or naphthyl.
- 7. A compound according to Claim 1 wherein R^2 is $-(CH_2)_n$ -cycloalkyl.
 - 8. A compound according to Claim 1 wherein R¹

$$O$$
 (CH₂)_n—phenyl or -SO₂-phenyl.

9. A compound according to Claim 1 wherein R² is —CH₂

10. A compound according to Claim 1 wherein R² is CH₃

CH₃

11. A compound of the Formula I

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wherein R^2 is -CH₂CH₂- aryl, -CH₂- cycloalkyl, -CH₂CH₂- cycloalkyl, or -CH₂CH₂- heteroaryl;

R¹ is

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$$R^{a}$$
, R^{b} , R^{c} , R

 R^a is -(CH₂)_n- aryl or -(CH₂)_n heteroaryl;

Rb is aryl or heteroaryl;

10 R^c is -CH₂ aryl or aryl;

Rd is hydrogen or C1-C6 alkyl;

Re is -CH₂ aryl or -CH₂ heteroaryl; and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

12. A compound according to Claim 11 wherein R¹ is

13. A compound according to Claim 11 wherein R¹ is

- 5 14. A compound according to Claim 11 wherein Re is -(CH₂)_n aryl.
 - 15. A compound according to Claim 14 wherein aryl is phenyl or naphthyl.
 - 16. A compound according to Claim 13 wherein Rb is aryl.
 - 17. A compound according to Claim 16 wherein is aryl is phenyl.
 - 18. The compounds:

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- 3-Benzyloxycarbonylamino-4-oxo-5-(2-phenylethanesulfonylamino)-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-(3-phenyl-propane-1-sulfonylamino)-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-phenylmethanesulfonylamino-pentanoic acid;
- 5-Benzenesulfonylamino-3-benzyloxycarbonylamino-4-oxopentanoic acid;
- 3-Benzyloxycarbonylamino-5-methanesulfonylamino-4-oxopentanoic acid;

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3-Benzyloxycarbonylamino-5-(naphthalene-1-sulfonylamino)-4-oxo-pentanoic acid;

		3-Benzyloxycarbonylamino-5-(2-cyclohexyl-ethanesulfonylamino)-
		4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(2-naphthalen-1-yl-
		ethanesulfonylamino)-4-oxo-pentanoic acid;
5		3-Benzyloxycarbonylamino-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(R)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(indan-1-ylmethanesulfonylamino)-
		4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(9-fluoro-9H-fluoren-9-
10		ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(S)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-(2-Acetylamino-3-methyl-butyrylamino)-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(S)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
15		3-(2-Acetylamino-propylamino)-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(S)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-(1,2,3,4-tetrahydro-1-oxo-isoquinoline-2-yl)-acetanino-
		5-benzenesulfonylamino-4-oxo-pentanoic acid;
		(S)-5-(Bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-3-[2-
20		(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-acetylamino]-pentanoic acid;
		(S)- 4-Oxo-3-[2-(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-
		acetylamino]-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid; and
		4-Oxo-3-[2-(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-acetylamino]-
		5-phenylmethanesulfonylamino-pentanoic acid.
25	19.	A method of inhibiting interleukin- 1β converting enzyme, the method
		comprising administering to a patient in need of inhibition of
		interleukin-1β converting enzyme a therapeutically effective amount of a
		compound of Claim 1

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- 20. A method of inhibiting Caspase-4, the method comprising administering to a patient in need of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 1.
- A method of treating or preventing stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 1.
 - 22. A method of treating inflammatory diseases, the method comprising administering to a patient having an inflammatory disease a therapeutically effective amount of a compound of Claim 1.
- 10 23. The method of Claim 22 wherein the inflammatory disease is arthritis.
 - 24. The method of Claim 22 wherein the inflammatory disease inflammatory bowel disease.
 - 25. A pharmaceutically acceptable composition that contains a compound of Claim 1.
- 15 26. A method of inhibiting interleukin-1β converting enzyme, the method comprising administering to a patient in need of inhibition of interleukin-1β converting enzyme a therapeutically effective amount of a compound of Claim 11.
- 27. A method of inhibiting Caspase-4, the method comprising administering to a patient in need of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 11.
 - 28. A method of treating or preventing stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 11.

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- 29. A method of treating inflammatory diseases, the method comprising administering to a patient having an inflammatory disease a therapeutically effective amount of a compound of Claim 11.
- 30. The method of Claim 29 wherein the inflammatory disease is arthritis.
- 5 31. The method of Claim 29 wherein the inflammatory disease is inflammatory bowel disease.
 - 32. A pharmaceutically acceptable composition that contains a compound of Claim 11.
- 33. A method of treating septic shock, the method comprising administering to a patient having septic shock a therapeutically effective amount of a compound of Claim 1.
 - 34. A method of treating septic shock, the method comprising administering to a patient having septic shock a therapeutically effective amount of a compound of Claim 11.
- 15 35. A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 1.

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- 36. A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 11.
- 37. A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 1.

- 38. A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 11.
- 39. A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 1.
 - 40. A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 11.
- 10 41. A compound of the Formula II

wherein

R¹ is

$$R^{a}$$
, R^{b} , R^{e} , R^{e} , R^{e} , R^{d} , R

15 R^a is -(CH₂)_n- aryl or -(CH₂)_n heteroaryl;

Rb is aryl or heteroaryl;

Rc is -CH2 aryl or aryl;

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Rd is hydrogen or C1-C6 alkyl;

Re is -CH₂ aryl or -CH₂ heteroaryl; and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

42. A compound according to Claim 41 wherein R¹ is

pe_O

43. A compound according to Claim 41 wherein R¹ is

- 44. A compound according to Claim 41 wherein Re is -(CH₂)_n aryl.
- 45. A compound according to Claim 41 wherein aryl is phenyl or naphthyl.
- 10 46. A compound according to Claim 41 wherein Rb is aryl.
 - 47. A compound according to Claim 46 wherein is aryl is phenyl.
 - 48. A method of inhibiting interleukin-1β converting enzyme, the method comprising administering to a patient in need of inhibition of interleukin-1β converting enzyme a therapeutically effective amount of a compound of Claim 41.
 - 49. A method of inhibiting Caspase-4, the method comprising administering to a patient in need of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 41.

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- 50. A method of treating or preventing stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 41.
- 51. A method of treating inflammatory diseases, the method comprising
 administering to a patient having an inflammatory disease a therapeutically
 effective amount of a compound of Claim 41.
 - 52. The method of Claim 51 wherein the inflammatory disease is arthritis.
 - 53. The method of Claim 51 wherein the inflammatory disease inflammatory bowel disease.
- 10 54. A method of treating septic shock, the method comprising administering to a patient having septic shock a therapeutically effective amount of a compound of Claim 41.
 - 55. A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 41.
 - 56. A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 41.
 - 57. A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 41.
 - 58. The compounds:

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3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid;

- 3-[2-(2-Benzyloxycarbonylamino-4-carboxy-butyrylamino)-3-methyl-butyrylamino]-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid;
- 3-{2-[4-Carboxy-2-(3-phenyl-propionylamino)-butyrylamino]-3-methyl-butyrylamino}-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-4-carboxy-butyrylamino)-3-methyl-butyrylamino]-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
- 3-{2-[4-Carboxy-2-(3-phenyl-propionylamino)-butyrylamino]-3-methyl-butyrylamino}-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
- 3-(2-{2-[2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino]-4-carboxy-butyrylamino}-3-methyl-butyrylamino)-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-pentanoic acid; and
- 3-(2-{2-[2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino]-4-carboxy-butyrylamino}-3-methyl-butyrylamino)-4-oxo-5-(2-phenylethanesulfonylamino)-pentanoic acid.

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